



Major hepatectomy for intrahepatic cholangiocarcinoma or colorectal liver metastases. Are we talking about the same story?☆



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ABSTRACT

Introduction: Major hepatectomy (MH) is often needed in the curative management of intrahepatic cholangiocarcinoma (IHCC) and colorectal liver metastases (CRLM). While similar outcomes could be expected after MH for IHCC and CRLM, outcomes seem worse after MH for IHCC. A better understanding of such differences might help improving perioperative outcomes but comprehensive analysis are lacking.

Methods: All patients undergoing curative intent MH for IHCC or CRLM from 2003 to 2009 were included from two dedicated multi-institutional datasets. Preoperative management and short-term outcomes after MH were first compared. Independent predictors of postoperative mortality and morbidity were identified.

Results: Among 827 patients, 333 and 494 patients underwent MH for IHCC and CRLM, respectively. Preoperative portal vein embolization was more frequently performed in the CRLM group ($p < 0.001$). MH in the IHCC group required more extended resection ($p < 0.001$). Postoperative mortality and severe morbidity rates were significantly higher in the IHCC group (7.2% vs. 1.2% and 29.7% vs. 11.1%, $p < 0.001$, respectively). Main causes for mortality were postoperative liver failure and deep surgical site infection. MH for IHCC was an independent risk factor for mortality ($p < 0.001$) and severe morbidity ($p < 0.001$). After propensity score matching (212 patients in each group), the aforementioned differences regarding outcomes remained statistically significant.

Conclusion: This study suggests that IHCC patients are inherently more at risk after MH as compared to CRLM patients. Considering that postoperative liver failure was the most frequent cause of death, preoperative planning might have been inadequate in the setting of IHCC while more complex/extended resections should be expected.

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Introduction

Hepatectomy stands as the cornerstone for the curative management of liver malignancies. Advances in perioperative management have translated in reduced mortality and morbidity overtime [1]. The advent of parenchymal-sparing hepatectomies has substantially decreased intraoperative blood loss and postoperative liver failure (POLF) [1–3]. Nevertheless, parenchymal sparing is not always achievable and major hepatectomy (MH) remains frequently required (51.2%–61.8%) with mortality rates ranging from 2 to 6.4%, according to largest series [1,3–5]. Regarding hepatic malignancies, MH is often required for IHCC (76.8%) and CRLM (58%) [6–8]. While similar outcomes could be expected after MH for IHCC or CRLM, mortality and morbidity rates after MH for IHCC (mortality: 6.4–9.9%, morbidity: 48.4–49.9%) are worse than for CRLM (mortality: 0–2%, morbidity: 16–32%) [9–13]. Whereas a better understanding of such differences might help improving perioperative management and outcomes, no comprehensive comparative study is currently available in the literature. This observation motivated the current study. Preoperative management and short-term outcomes after MH for IHCC or CRLM were first compared. The secondary objective was to identify independent predictors of postoperative mortality and morbidity in patients undergoing MH whether for IHCC or CRLM.

Methods

Study population

Data on all patients who underwent MH with curative intent for IHCC or CRLM from January 2003 to January 2009 at 24 hepatobiliary centers were collected from two dedicated nationwide datasets. Both datasets were collected under the supervision of the French Surgical Association (Association Française de Chirurgie) after institutional approval. Details of the methodology have been reported previously [7,12]. In brief, palliative-intent resection such as R2 resection were excluded. Regarding IHCC, mixed cholangiocarcinoma–HCCs and cholangiocarcinomas arising from the perihilar biliary tract or gallbladder were excluded. MH was defined as the resection of at least three Couinaud segments [14]. Extended hepatectomy was defined as the resection of five Couinaud segments or more.

Data collection

Preoperative variables included demographics, ASA grade, and data regarding preoperative management such as portal vein embolization (PVE), biliary drainage and neoadjuvant treatment. Operative variables included the need for pedicle clamping, intraoperative blood transfusion and duration of operation. Combined resections of vascular, biliary or extrahepatic structures were also recorded, as well as whether lymphadenectomy was performed. Underlying liver was considered based on pathologic results of the non-tumoural parenchyma. Briefly, the presence of steatosis, steatohepatitis, sinusoidal dilatation were considered as defined based on their respective definitions [15,16]. Similarly, the presence of fibrosis and cirrhosis in the non-tumoural liver was collected. Postoperative mortality and morbidity were measured within 90 days of surgery. Any postoperative event occurring within 90 days and deemed as leading to deviation from the normal postoperative course was considered a complication and was graded according to the Dindo–Clavien classification [17]. Grade 3 or more complication was considered as severe morbidity. In patients with multiple complications, the highest grade was retained for analysis. Abdominal complications were dichotomized into hepatic and

non-hepatic. The former included postoperative liver failure, biliary fistula, haemorrhage according to the definitions of the International Study Group of Liver Surgery [18–20], cholangitis defined as fever and leucocytosis requiring antibiotics or biliary drainage, and vascular thrombosis. Abdominal non-hepatic complications included postoperative ileus, gastroparesis, intra-abdominal infection, gastrointestinal bleeding and wound dehiscence/infection. Non-abdominal complications comprised pulmonary complications (pneumonia, pleural effusion, respiratory insufficiency, pulmonary embolism), urinary complications (urinary tract infections, urinary retention) and other types, including cardiac complications, deep vein thrombosis, acute renal failure and catheter-related infections.

Statistical analysis

Categorical variables, presented as numbers and percentages, were compared using the χ^2 test. Continuous variables with a normal distribution are presented as mean (s.d.) and non-normally distributed variables as median (range); and were compared using respectively *t*-test and Mann–Whitney *U* test. Comparisons between MH for IHCC or CRLM were performed regarding preoperative and intraoperative data and postoperative outcomes in the full cohort and in a matched cohort. Univariable and multivariable regression analysis were used to identify independent predictive factors of mortality and morbidity in the full cohort. Patients undergoing MH for IHCC were then matched to those undergoing MH for CRLM using the propensity score matching (PSM) method. The propensity score for an individual was calculated using a multivariable logistic regression model including the following variables: age, gender, body mass index, ASA score, preoperative total bilirubin level, preoperative portal vein embolization, presence of underlying disease, resection extent, portal lymphadenectomy, combined vascular resection, combined biliary resection and intraoperative transfusion. Of note, variables such neoadjuvant therapy and repeat hepatectomy were not used for PSM because they are inherently associated with the management of CRLM. Using a standard calliper width of 0.2, IHCC patients were matched without replacement to the closest matching propensity score in CRLM patients in a 1:1 ratio. Two-tailed *p* values < 0.050 were considered statistically significant. Statistical analyses were carried out using SPSS Statistics 23.0 (SPSS Inc., Chicago, IL, USA) and R Studio version 3.4.3 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Study population before matching

Over the study period, 434 and 1243 patients underwent hepatectomy for IHCC and CRLM respectively. Among them, 333 (76.7%) and 494 (39.7%) patients who underwent MH for IHCC and CRLM respectively were included in the study cohort. Patients in the IHCC group were significantly older ($p < 0.001$) and presented higher total bilirubin levels ($p < 0.001$), requiring more preoperative biliary drainage ($p < 0.001$) (Table 1). In contrast, patients who underwent MH for CRLM were significantly frailer considering their ASA status ($p = 0.038$) and received significantly more often prehepatectomy PVE and neoadjuvant therapy ($p < 0.001$).

In the IHCC group, MH were significantly more often extended ($p < 0.001$) and combined with biliary or vascular resection ($p < 0.001$), requiring longer operative time ($p = 0.001$), more vascular clamping and transfusion as compared to the CRLM group (Table 1). MH was performed by laparoscopic approach in 44 patients (8.4%) with CRLM.

Table 1

Descriptive data from consecutive patients who underwent major hepatectomy between 2003 and 2009 (n = 827).

	CRLM (n = 494)	IHCC (n = 333)	P
Preoperative data			
Age, years	61.3 (11)	64.2 (11.5)	<0.001
Age > 70 years	106 (21.5%)	114 (34.2%)	<0.001
Gender	Male	155 (46.5%)	0.006
	Female	178 (53.5%)	
BMI, kg/m ²	25.4 (4.2)	25.3 (4.5)	0.826
ASA > 2	77 (15.6%)	35 (10.5%)	0.038
Preoperative total bilirubin, μmol/l	12 (11.5)	29.5 (64.6)	<0.001
Preoperative PVE	135 (27.3%)	36 (10.8%)	<0.001
Neoadjuvant therapy	252 (51%)	22 (6.6%)	<0.001
Intraoperative data			
Laparoscopic liver resection	44 (8.4%)	Unk	-
Repeat hepatectomy	106 (21.5%)	15 (4.5%)	<0.001
Extended hepatectomy	78 (15.8%)	128 (38.4%)	<0.001
Portal lymphadenectomy	31 (6.3%)	203 (61%)	<0.001
Combined biliary resection	8 (1.6%)	70 (21%)	<0.001
Combined vascular resection	18 (3.6%)	40 (12%)	<0.001
Operative time, minutes	274 (113)	312 (132)	0.001
Pedicle clamping	340 (68.8%)	264 (79.3%)	0.001
Intraoperative transfusion	103 (20.9%)	106 (31.8%)	<0.001
Postoperative data			
Length of stay, days	14.4 (10.1)	18.5 (12.7)	<0.001
Postoperative mortality	6 (1.2%)	24 (7.2%)	<0.001
Postoperative morbidity	216 (43.7%)	170 (51.1%)	0.04
Postoperative severe morbidity	55 (11.1%)	99 (29.7%)	<0.001
Morbidity details ^a			
Abdominal	109 (22.1%)	121 (36.3%)	<0.001
Hepatic	72 (14.6%)	117 (35.1%)	<0.001
Biliary fistula	36 (7.3%)	53 (15.9%)	<0.001
POLF	33 (6.7%)	40 (12%)	0.009
Haemorrhage	3 (0.6%)	24 (7.2%)	<0.001
Non hepatic	90 (18.2%)	103 (30.9%)	<0.001
Deep SSI	63 (12.8%)	55 (16.5%)	0.130
Non abdominal	101 (20.4%)	58 (17.4%)	0.322
Adjuvant therapy	227 (46%)	96 (28.8%)	<0.001

Continuous variables are expressed as mean (standard deviation); categorical variables are expressed as n (%).

ASA, American Society of Anaesthesiology; BMI, body mass index; POLF, postoperative liver failure; PVE, portal vein embolization; SSI, surgical site infection.

^a Patient may have more than one complication.

While mean tumour size of the largest lesion was significantly larger in the IHCC group (7.5 cm, SE 4.1) as compared to the CRLM group (4.1 cm, SE 3.4; $p < 0.001$), disease was more often multifocal in the CRLM group as compared to the IHCC group ($p < 0.001$). Complete R0 resection rate did not differ between both groups (75.4% vs. 73.8%, $p = 0.667$, respectively). Regarding the underlying liver parenchyma, 188 (56.5%) and 251 (50.8%) patients presented with the existence of underlying liver injuries in the IHCC and CRLM groups respectively ($p = 0.118$, Table 2).

Postoperative outcomes before matching

In the full population (n = 827), overall postoperative mortality,

Table 2

Pathologic data from consecutive patients who underwent major hepatectomy between 2003 and 2009 (n = 827).

	CRLM (n = 494)	IHCC (n = 333)	P
Underlying liver parenchyma ^a	251 (50.8%)	188 (56.5%)	0.118
Steatosis	133 (26.9%)	93 (27.9%)	0.668
Steatohepatitis	7 (1.4%)	10 (3%)	0.136
Sinusoidal dilatation	64 (13%)	12 (3.6%)	<0.001
Fibrosis	107 (21.7%)	95 (28.5%)	0.026
Cirrhosis	2 (0.4%)	13 (3.9%)	<0.001
Multiple	58 (11.7%)	43 (12.9%)	0.665

^a One same patient could have several underlying liver lesions.

morbidity and severe morbidity rates were 3.6%, 46.7% and 18.6%. Among postoperative deaths (n = 30), POLF (n = 17, 56.7%) and deep surgical site infection (n = 10, 33.3%) were involved while non-abdominal complications (n = 15) occurred in 50%. Postoperative mortality rate was significantly higher in the IHCC group (n = 24, 7.2%) than in the CRLM group (n = 6, 1.2%, $p < 0.001$). Similarly, morbidity and severe morbidity rates were significantly higher in the IHCC group (51.1% vs. 43.7%, $p = 0.04$ and 29.7% vs. 11.1%, $p < 0.001$, respectively). Details about morbidity after HM are listed in Table 1. Median length of stay was significantly longer in the IHCC group ($p < 0.001$).

Perioperative variables associated with mortality and severe morbidity in the full population are shown in Tables 3 and 4. Upon multivariable analysis, MH for IHCC was the only independent risk factor of postoperative mortality (OR = 5.747, CI95% 2.299–14.368; $p < 0.001$) while the need for combined vascular resection tended toward statistical significance (OR = 2.374, CI95% 0.909–6.201; $p = 0.078$). Regarding severe morbidity, MH for IHCC (OR = 3.117, CI95% 2.147–4.523; $p < 0.001$) and the need for intraoperative transfusion (OR = 2.684, CI95% 1.837–3.923; $p < 0.001$) were identified as independent predictors of severe morbidity.

Postoperative outcomes after matching

After propensity score adjustment, both groups were comparable in terms of preoperative and intraoperative variables (212

Table 3
Perioperative variables associated with 90 days postoperative mortality in univariable analysis.

	POD90+ (n = 30)	POD90-(n = 797)	P
Age, years	64.8 (11.2)	61.8 (11)	0.150
Age>70 years	11 (36.7%)	209 (26.2%)	0.210
Gender			0.137
	Male	414 (51.9%)	
	Female	383 (48.1%)	
BMI, kg/m ²	25.6 (3.9)	25.3 (4.3)	0.428
ASA>2	5 (16.7%)	107 (13.4%)	0.587
Preoperative total bilirubin, μmol/l	41.7 (91)	19.5 (43.5)	0.015
Preoperative biliary drainage	-	16 (2%)	>0.999
Preoperative PVE	5 (16.7%)	166 (20.8%)	0.818
Underlying steatosis on pathology	10 (33.3%)	215 (27%)	0.412
Underlying SD on pathology	1 (3.3%)	75 (9.4%)	0.513
Underlying fibrosis on pathology	12 (40%)	190 (23.8%)	0.052
Underlying cirrhosis on pathology	2 (6.7%)	13 (1.6%)	0.100
Neoadjuvant therapy	3 (10%)	271 (34%)	0.005
Repeat hepatectomy	1 (3.3%)	120 (15.1%)	0.109
Hepatectomy for IHCC	24 (80%)	309 (38.8%)	<0.001
Extended hepatectomy	13 (43.3%)	193 (24.2%)	0.029
Portal lymphadenectomy	8 (26.7%)	226 (28.4%)	>0.999
Combined biliary resection	8 (26.7%)	70 (8.8%)	0.005
Combined vascular resection	6 (20%)	52 (6.5%)	0.014
Operative time, minutes	287 (156)	287 (120)	0.577
Pedicle clamping	24 (80%)	580 (72.8%)	0.530
Intraoperative transfusion	12 (40%)	197 (24.7%)	0.084

Continuous variables are expressed as mean (standard deviation); categorical variables are expressed as n (%).

ASA, American Society of Anaesthesiology; BMI, body mass index; IHCC, intrahepatic cholangiocarcinoma; PVE, portal vein embolization; SD, sinusoidal dilatation Table 4. Perioperative variables associated with 90 days severe morbidity in univariable analysis.

Table 4
Perioperative variables associated with 90 days severe morbidity in univariable analysis.

	Severe morbidity (n = 154)	No severe morbidity (n = 673)	P
Age, years	63 (11.3)	61.7 [11]	0.123
Age>70 years	51 (33.1%)	169 (25.1%)	0.054
Gender			0.372
	Male	345 (51.7%)	
	Female	325 (48.3%)	
BMI, kg/m ²	25.4 (4.2)	25.4 (4.2)	0.813
ASA>2	22 (14.3%)	90 (13.4%)	0.794
Preoperative total bilirubin, μmol/l	32.9 (73.7)	17.3 (36)	<0.001
Preoperative biliary drainage	7 (4.5%)	9 (1.3%)	0.017
Preoperative PVE	23 (14.9%)	148 (22%)	0.060
Underlying steatosis on pathology	44 (28.6%)	181 (26.9%)	0.689
Underlying SD on pathology	15 (9.7%)	61 (9.1%)	0.759
Underlying fibrosis on pathology	41 (26.6%)	161 (23.9%)	0.469
Underlying cirrhosis on pathology	3 (1.9%)	12 (1.8%)	0.749
Underlying cholestasis on pathology	8 (9.1%)	18 (8.5%)	0.825
Neoadjuvant therapy	31 (20.1%)	243 (36.1%)	<0.001
Repeat hepatectomy	14 (9.1%)	107 (15.9%)	0.032
Hepatectomy for IHCC	99 (64.3%)	234 (34.8%)	<0.001
Extended hepatectomy	50 (32.5%)	156 (23.2%)	0.018
Portal lymphadenectomy	63 (40.9%)	171 (25.4%)	<0.001
Combined biliary resection	27 (17.5%)	51 (7.6%)	<0.001
Combined vascular resection	18 (11.7%)	40 (5.9%)	0.021
Operative time, minutes	333 (140)	278 (115)	<0.001
Pedicle clamping	116 (75.3%)	488 (72.5%)	0.546
Intraoperative transfusion	68 (44.2%)	141 (21%)	<0.001

Continuous variables are expressed as mean (standard deviation); categorical variables are expressed as n (%).

ASA, American Society of Anaesthesiology; BMI, body mass index; IHCC, intrahepatic cholangiocarcinoma; PVE, portal vein embolization; SD, sinusoidal dilatation.

patients in each group, Table 5). Overall postoperative mortality, morbidity and severe morbidity rates were 4.2%, 46.5% and 21.5%. Among postoperative deaths (n = 18), POLF (n = 12, 66.7%) and deep surgical site infection (n = 7, 38.9%) were involved while non-abdominal complications (n = 10) occurred in 55.6%. Postoperative mortality rate was significantly higher in the IHCC group (n = 14, 6.6%) than in the CRLM group (n = 4, 1.9%, p = 0.027). Similarly, severe morbidity was significantly higher in the IHCC group (28.8% vs. 14.2%, p < 0.001) while there was no difference in terms of overall morbidity between both groups (p = 0.846). Details about morbidity after MH are listed in Table 5. POLF occurred in 38

patients (9%) and tended to be more observed in the IHCC group (p = 0.089). Median length of stay was significantly longer in the IHCC group (p = 0.008).

Discussion

Differences in characteristics and outcomes after MH for CRLM and IHCC reported in the literature are confirmed in this multi-center study. More importantly, the current study is the first to specifically focus on the comparison of MH for CRLM versus IHCC. This may bring some comprehensive insights to explain these

differences and to improve management and outcomes.

Intraoperatively, patients in the IHCC group required significantly more extended hepatectomy, combined biliary and vascular resections translating in longer operative time and higher need for intraoperative transfusion. Such results are to be related to tumour characteristics. IHCC tends to be often diagnosed at late stage with large tumour, central location, and contact with the hepatic hilum and the retrohepatic inferior vena cava. Tumour size was significantly higher in the IHCC group. Consequently, more extended and complex hepatectomies were required to achieve complete resection in patients with underestimated chronic liver disease. This observation might explain the need for longer operative time and higher transfusion rate in the IHCC group. Indeed, hepatectomy complexity owing to extended resection and combined vascular or biliary resection are reported as associated to higher operative time, blood loss and transfusion rate in both CRLM and IHCC populations [21–23]. Additionally, hepatectomy extent, biliary and vascular reconstructions, intraoperative blood loss and transfusion have already been identified as independent risk factors for mortality and morbidity after MH [1,3,5,24–27]. All these variables along with age, preoperative jaundice and underlying liver injury were identified as risk factors for mortality and morbidity on univariable analysis (Tables 3 and 4). Not surprisingly, portal lymphadenectomy was significantly more performed during MH for IHCC. Yet, while vascular and biliary injury during portal lymphadenectomy may lead to specific morbidity such as bleeding, biliary ischemia or lymphatic leak, portal lymphadenectomy was not independently associated with postoperative outcomes.

In the current study, POLF was observed in 8.8% and accounted

for 56.7% of postoperative deaths. Similar results were found in the matched population. Consequently, POLF was significantly associated with postoperative mortality (data not shown). Comparing MH for IHCC to MH for CRLM, POLF occurred significantly more often after MH for IHCC. Before MH, prehepatectomy planning is paramount to anticipate resection extent and to prevent POLF by optimizing the future liver remnant through portal vein embolization (PVE) and biliary drainage in case of estimated insufficient future liver remnant function or obstructive jaundice, respectively [28,29].

Regarding preoperative planning, a paradox has to be pointed out. While preoperative PVE was significantly less performed in the IHCC group, MH was significantly more extended and the underlying liver significantly more often injured in the IHCC group, with a higher rate of cirrhosis. One can hypothesize that preoperative planning was inadequate in the IHCC group by underestimating the real extent of the lesion to the parenchyma and hilar structures and inaccurately assessing the underlying liver. Such an inaccurate planning may have led to more invasive procedures in more diseased patients than anticipated, thus translating in high mortality and morbidity rates. Indeed, using root cause analysis, Khaoudy et al. reported that insufficient evaluation of the tumour extent resulting in a more extended procedure than expected was the main cause of death after hepatectomy [30]. As compared to CRLM, IHCC are known as large and infiltrative tumours. Their extent through the liver parenchyma could be challenging to delineate on imaging, leading to unanticipated intraoperative findings requiring more extended resection than initially planned [31]. In this regard, accurate preoperative tumour mapping for

Table 5

Descriptive data from matched patients who underwent major hepatectomy for IHCC (n = 212) or CRLM (n = 212).

	CRLM (n = 212)	IHCC (n = 212)	P
Preoperative data			
Age, years	61.8 (11.2)	63.2 (11)	0.196
Gender	Male	97 (45.8%)	0.331
	Female	115 (54.2%)	
BMI, kg/m ²	25.2 (3.9)	25.7 (4.1)	0.330
ASA>2	30 (14.2%)	23 (10.8%)	0.378
Preoperative total bilirubin, μmol/l	12.4 (16)	16.2 (21.5)	0.181
Preoperative PVE	34 (16%)	26 (12.3%)	0.329
Neoadjuvant therapy	114 (53.8%)	13 (6.1%)	<0.001
Underlying liver disease	52 (24.5%)	59 (27.8%)	0.508
Intraoperative data			
Repeat hepatectomy	36 (17%)	12 (5.7%)	<0.001
Extended hepatectomy	47 (22.2%)	54 (25.5%)	0.494
Portal lymphadenectomy	30 (14.2%)	37 (17.5%)	0.425
Combined biliary resection	6 (2.8%)	12 (5.7%)	0.228
Combined vascular resection	7 (3.3%)	13 (6.1%)	0.252
Operative time, minutes	281 (111)	284 (120)	0.843
Pedicle clamping	138 (65.1%)	169 (79.7%)	0.006
Intraoperative transfusion	44 (20.8%)	51 (24.1%)	0.485
Postoperative data			
Length of stay, days	13.9 (9.6)	16.7 (11)	0.008
Postoperative mortality	4 (1.9%)	14 (6.6%)	0.027
Postoperative morbidity	100 (47.2%)	97 (45.8%)	0.846
Postoperative severe morbidity	30 (14.2%)	61 (28.8%)	<0.001
Morbidity details^a			
Abdominal	49 (23.1%)	70 (33%)	0.030
Hepatic	39 (15.8%)	77 (31.2%)	<0.001
Biliary fistula	17 (8%)	30 (14.2%)	0.006
POLF	14 (6.6%)	24 (11.3%)	0.089
Haemorrhage	1 (0.5%)	14 (6.6%)	<0.001
Non hepatic	41 (19.3%)	62 (29.2%)	0.023
Deep SSI	28 (13.2%)	31 (14.6%)	0.779
Non Abdominal	48 (22.6%)	35 (16.5%)	0.142

Continuous variables are expressed as mean (standard deviation); categorical variables are expressed as n (%).

ASA, American Society of Anaesthesiology; BMI, body mass index; POLF, postoperative liver failure; PVE, portal vein embolization; SSI, surgical site infection.

^a Patient may have more than one complication.

hepatectomy planning stands as of major interest to improve hepatectomy safety [32]. Additionally, the nature of the underlying liver parenchyma could be routinely assessed through preoperative imaging or biopsy of non tumour tissue, especially in the setting of IHCC where underlying liver injury is often preexisting. Taken altogether, these data suggest that the implementation of a tailored preoperative planning with tumour mapping and systematic future liver remnant assessment and optimization using PVE for a planned extended resection as currently advocated for perihilar cholangiocarcinoma might be of benefit in the setting of large and/or centrally located IHCC. Such an approach would decrease the risk of performing more extended resection than preoperatively planned.

However, even after PSM (Table 5), mortality and severe morbidity remained significantly higher in the IHCC group. This suggests that IHCC patients might be inherently at higher operative risk as compared to CRLM patients with unidentified risk factors.

In addition to its retrospective nature, some limitations of the present study warrant discussion. First, the current study raises the point of inadequate preoperative planning leading to unplanned extended and complex hepatectomy for IHCC. While data on the actual resection were available, data on the initially planned resection by the attending surgeon in each case was lacking. This data would have been of great value to evaluate the rate of inadequate planning in each group. Second, the study time period from 2003 to 2009 may implicate lead-time bias especially regarding surgical approach and techniques that have evolved overtime. Cloyd et al. have recently shown the impact of the evolution of liver surgery on outcomes [27]. However, outcomes in the current study are comparable to large series focused on similar time periods [1,5,24,27]. Third, both groups were significantly different in terms of preoperative, intraoperative and postoperative data. Such multiple differences might have hampered the identification of independent predictors. However, confounding factors were handled using multivariable logistic regression models where MH for IHCC remained an independent risk factor for both mortality and morbidity. Additionally, matching on potential confounding factors showed that differences in postoperative outcomes remained unchanged as observed in the unmatched cohort. This finding underlines that even beyond preoperative management, patients submitted to MH for IHCC are inherently at higher operative risk than for CRLM. Finally, performing MH under laparoscopy is nowadays widespread but remains challenging and under evaluation. While MH was performed by laparoscopy in 8.4% of the CRLM group, no data regarding the use of laparoscopy was available in the IHCC group. However, given the study period, feasibility and outcomes of laparoscopic MH would be better appraised in more recent cohorts. While the laparoscopic approach for CRLM has been extensively evaluated, evaluation is still needed in the setting of IHCC [33–35].

In conclusion, this comparative study of MH for IHCC or CRLM confirmed significantly higher mortality and morbidity in patients operated on for IHCC. These differences regarding outcomes are multifactorial but preoperative planning for assessing and optimizing the future liver remnant remains key for controlling on these factors. Notably, PVE and underlying liver assessment should be routinely considered before MH, especially in the setting of IHCC.

Declarations of interest

None

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